Medical and Pediatric Oncology 28:304–309 (1997)

Osteoblastoma Response to Radiotherapy and Chemotherapy

Semha Berberoğlu, MD,[1]* Aynur Oğuz, MD, Erkin Arıbal, MD,[2] and Omur Ataoğlu, MD[3]

Osteoblastoma is a rare primary bone tumor that is curable by complete excision. There are few data about the effectiveness of chemotherapy or radiotherapy in the treatment of recurrent osteoblastoma. We report a 13-year-old girl with recurrent osteoblastoma who, after in complete surgical excision, responded to treatment with radiotherapy and later with chemotherapy. Surgery remains the treatment of choice for osteoblastoma. Radiotherapy and chemotherapy either alone or together may be useful in selected patients with recurrent, aggressive tumor or in patients with surgically unresectable disease. **Med. Pediatr. Oncol. 28:304–309.**

Key words: osteoblastoma; recurrent; treatment; childhood

INTRODUCTION

Osteoblastoma is a rare benign primary bone tumor seen primarily in children and young adults [1,2]. It comprises approximately 1% of primary bone tumors [3]. Approximately 40% of osteoblastomas occur in the spine, with the majority of these localized to the posterior elements. A review of the literature revealed that cases of osteoblastoma primarily involving the vertebral body are exceedingly rare [4,5]. Typical osteoblastoma is curable by complete excision. Recurrence usually results from incomplete removal or histologic confusion with low-grade osteosarcoma [6,7]. For recurrent osteoblastoma, the mainstay of therapy is re-excision. Radiation therapy has been used infrequently but has provided local control and long-term, disease-free survival in some patients [8]. There are few data about the responsiveness of recurrent osteoblastoma to chemotherapy.

We report a child with recurrent osteoblastoma involving the body and posterior elements of C4, C5, and C6. The tumor responded to treatment with radiotherapy but recurred 2 years later. After treatment with cisplatin and doxorubicin, tumor regressed and there has been no tumor regrowth in the 18 months since discontinuing chemotherapy.

CASE REPORT

In January 1991, a 13-year-old girl was admitted to the hospital with pain in the neck; vertigo; lack of neck, arm, and leg movements; constipation; and disability to urinate. She had C5 compression fracture and brachial plexus lesion after a trauma to the neck region 3 years earlier. Her pain increased as time passed. After a second trauma that occurred 1 month before presentation, quadriplegia occurred gradually. On physical examination, neck movements were painful and restricted. There was a 6 × 8 cm solid, fixed mass on the left cervical region, behind the left sternocleidomastoid muscle. Hypoesthesia up to C4 and 90% weakness of the four extremities was present. There was muscle atrophy, especially on the upper extremities. Deep tendon reflexes (DTR) were decreased at the upper extremities and increased at the lower extremities. Bilateral Babinsky test was positive, and neurogenic bladder was present.

Plain radiographs of the cervical spine showed a mass arising in the left posterior elements of the C5 vertebra and expanding to C4 and C6 vertebral posterior elements. The lesion also showed expansion to the surrounding soft tissues, with the destruction of the cortex and demonstrated matrix mineralization. The fifth cervical vertebral body was compressed. On computed tomography (CT) scan, a lobulated mass extending into the C4, C5, and C6 vertebral bodies and expanding into the prevertebral space was demonstrated (Fig. 1). On magnetic resonance imaging (MRI), the lesion was hypointense on T1-weighted images (Fig. 2, top) and was of mixed intermediate-signal intensity signal void rim on T2-weighted images (Fig. 2, bottom left). The C4, C5, and C6 vertebral bodies were of low-signal intensity on T1-weighted images, and the intervertebral disc spaces were narrowed (Fig. 2, bottom right). The cord was compressed and showed high-signal intensity on T2-weighted images.

In January 1991, the first operation was performed and the portion of the tumor adherent to the corpus of the

[1]Departments of Pediatric Oncology and [2]Radiology, Oncology Hospital, and the [3]Departments of Pediatric Oncology and Pathology Gazi University, Ankara, Turkey.

Received 4 December 1995; Accepted 18 March 1996

*Correspondence to: Semha Berberoğlu, MD, Department of Pediatric Oncology, Oncology Hospital, Mesa Koru Sitesi, Sedir Sok 2/C 06798, Ankara, Turkey.

Fig. 1. Axial CT image (January 1991) at the level of C5 vertebra. A calcified mass is seen arising from C5 vertebral body and left posterior element. The spinal canal is narrowed.

C4–C6 vertebrae was partially excised. The first specimen was fixed in 19% formalin and subsequently was decalcified. Sections obtained from paraffin blocks were stained with hematoxylin-eosin. The histologic examination showed large mineralized bone structures resembling the mosaic pattern in Paget's disease. A woven bone pattern was observed in polarized light microscopy. A scanty stroma and few osteoblasts were observed in these areas. There were also areas rich in osteoid and newly formed bone alternating with areas containing large mineralized bone structures described above. Dilated capillary vessels and areas of hemorrhage were prominent in the loose connective tissue stroma. Thin osteoid trabeculae were rimmed by osteoblasts, and in some areas small groups of osteoblasts were observed between the osteoid fragments. There was no significant atypia or mitotic activity in the osteoblasts or in the fibroblastic cells of the stroma. Several multinuclear giant cells were observed in areas adjacent to the bony structures (Fig. 3). There were no appreciable epithelioid osteoblasts. A diagnosis of benign osteoblastoma was made.

In August 1991, a second operation was performed because of the detoriation of clinical symptoms. CT scan of the cervical spine showed a recurrent mass of 5.5 cm in diameter expanding into the prevertebral space and spinal canal. The stenosis of the spinal canal was more severe. Ossification of the tumor was evident. Only partial re-excision of the mass (less than 50%) and laminectomy could be achieved. Pathologic diagnosis was unchanged.

In November 1991, the patient received 5000 cGy radiotherapy with Co 60 to the cervical region. During the following 2 years, neck pain decreased and the patient was able to walk. The mass in the cervical region remained without further shrinkage. In February 1993, neck pain began to increase and there was detoriation in clinical symptoms. On CT examination, the mass was the same size as on previous CT examinations, but ossification of the mass was more prominent. On MRI, pathologic low-signal intensity of the affected vertebral bodies was replaced by the high-signal intensity of the fatty bone marrow on T1-weighted images. Edema was evident in the surrounding muscle tissues.

In September 1993, the patient was admitted to the hospital with neck pain unresponsive to medication. Results of physical examination showed weakness and decreased deep tendon reflexes of the four extremities. Bowel and bladder function were normal. Lateral cervical spine radiography showed a dense calcified mass between C4 and C6 levels (Fig. 4). Chemotherapy with cisplatin, 120 mg/m^2/day, and doxorubicin, 30 mg/m^2/day $\times$ 2 days, was begun in September 1993. Neck pain decreased dramatically; on physical examination, it was found that the cervical mass was beginning to shrink. Chemotherapy was continued for 8 months, and the patient received six courses of therapy.

In December 1993 on control CT examination, the mass was limited and totally ossified (Fig. 5). The lytic lesions in the vertebral bodies also showed ossification.

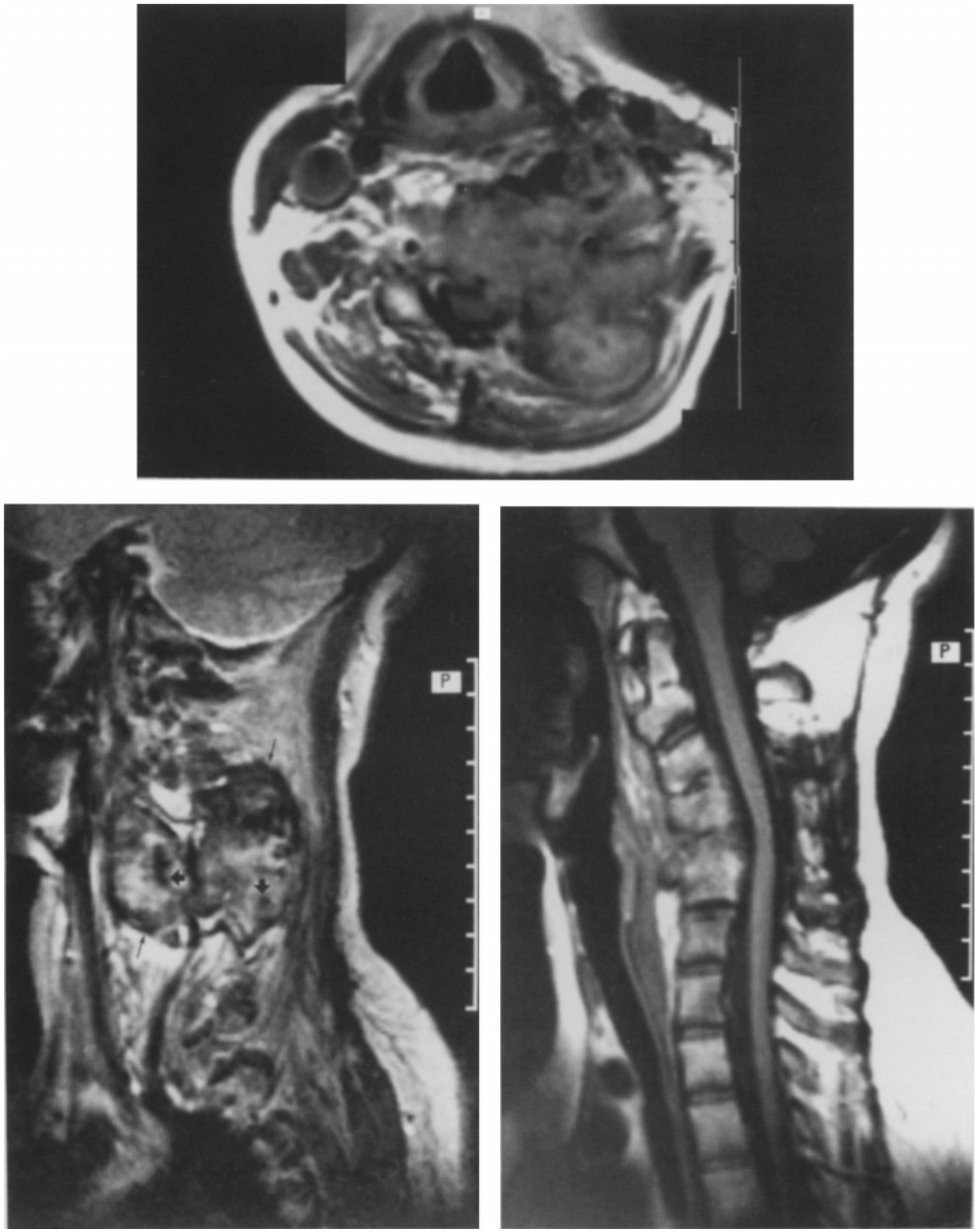

Fig. 2. **(Top)** T1-weighted axial MRI (January 1991) at the level of C5 vertebra. The mass is of low-signal intensity. The mass shows expansion into the prevertebral space and spinal canal. There is slight compression of the spinal cord. **(Bottom left)** T2-weighted left paramedian sagittal image. The mass is of mixed intermediate-signal intensity. Signal void foci (bold arrows) are seen in the mass, and the mass is surrounded with a signal void rim (narrow arrows). Note that the left vertebral artery is surrounded by the mass. **(Bottom right)** T1-weighted median sagittal image. C3, C4, and C5 vertebral bodies show low-signal intensity. Intervertebral disk spaces are narrowed. Kyphosis is present due to C5 vertebral body compression, and the spinal canal is narrowed.

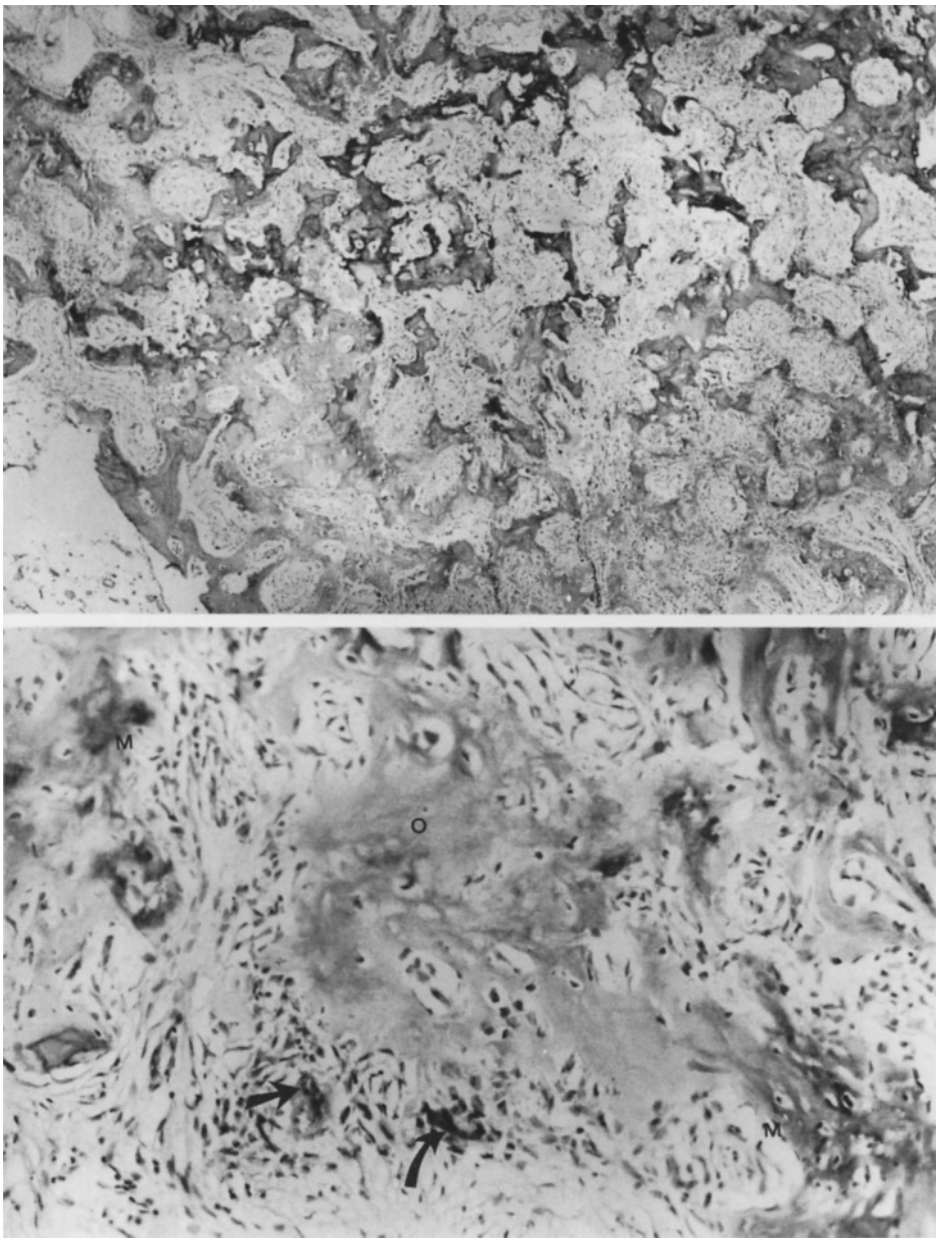

Fig. 3. **(Top)** A panaromic histopathologic view of the case presented. Hematoxylin-eosin, ×40. **(Bottom)** Osteoid (O) and mineralised bone (M) in a fibrous stroma. Multinuclear cells (arrows) are also present. Hematoxylin-eosin, ×200.

In April 1994, chemotherapy was stopped. On CT scan, there was intensive calcification and ossification and a slight decrease in the size of the mass when compared with previous scans.

The patient is currently pain free. There is no residual weakness. Physical examination shows that the left cervical mass continues to shrink, and lateral cervical radiographs show increasing calcification and ossification at the lesion site.

DISCUSSION

Approximately 40% of osteoblastomas occur in the spine, with the majority of these localized to the posterior elements, thereby facilitating surgical removal [9–13]. In approximately 14% of cases, there is involvement of the vertebral body alone [2]. Wide en bloc excision of the lesion is the recommended treatment. The anatomic location and size of our patient's tumor made complete resection more difficult.

The main histopathologic differential diagnosis in our patient had to be made with osteosarcoma. The absence of mitotic figures, lack of significant cellular atypia, thick osteoid and woven bone, and vascularized stroma are the features that are helpful in arriving at the correct diagnosis [14]. The presence of a cartilaginous matrix was once believed to exclude osteoblastoma in favor of osteosarcoma, but now it is known that this is not a reliable indicator of malignancy [15]. Although considered a be-

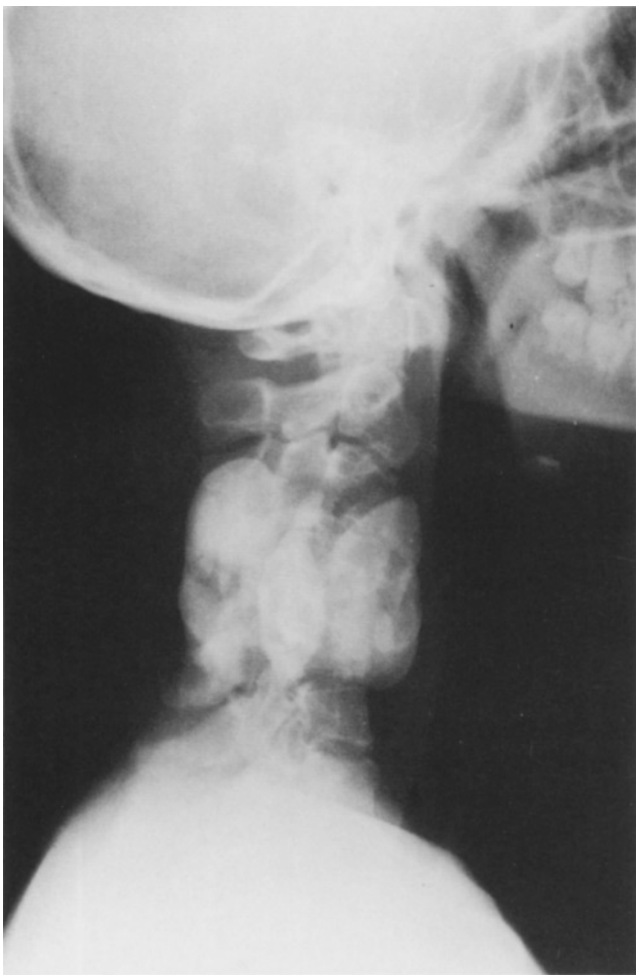

Fig. 4. Lateral radiograph of cervical spine (September 1993). A heavily calcified mass is seen between C3 and C5 vertebrae.

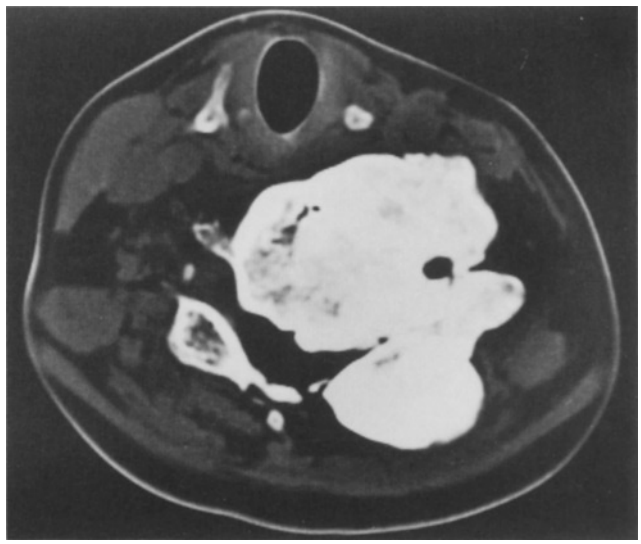

Fig. 5. Axial CT image of the mass (December 1993). The mass is ossified.

nign neoplasm, osteoblastoma may show sarcomatous transformation [16]. This phenomenon is generally accepted; however, there is always the possibility of undersampling an osteosarcoma that can contain areas indistinguishable from an osteoblastoma.

Osteoid osteoma is another lesion with pathologic features that should be considered in the differential diagnosis; Schajowicz and Lemos also considered both tumors to be osteoblastomas [17]. However, osteoid osteoma classically is smaller than 2 cm, radiologically presents with constant perifocal osseous reaction, and lacks a defined soft tissue mass. Histopathologically, there is scanty stromal reaction and rare multinucleated giant cells [14]. The absence of a central nidus in osteoblastoma is another distinguishing feature.

Aggressive osteoblastoma shows a tendency for local invasion and recurrence, but does not show metastasis. It has histologically typical osteoblastoma areas and epithelioid-like structures formed by osteoblasts with large cytoplasm [18]. However, in a series of 306 osteoblastomas, some of these tumors showed an aggressive course, but most did not [19]. The tumors involving the central neuraxis were found to be associated with greater morbidity and mortality, and it was concluded that an aggressive behavior is within the biologic spectrum of osteoblastomas. It was also concluded that histopathology alone does not appear to be a reliable predictor of aggressiveness.

The radiologic findings of osteoblastoma have been defined previously [3,20–22]. Our findings are similar to those described in the literature. The mass was of low-signal intensity on T1-weighted images and was of mixed intermediate-signal intensity on T2-weighted images. We believe that the intermediate-signal intensity of the mass on T2-weighted images was due to low water content and matrix mineralization of the tumor. The ossified rim of the mass on CT scan was of signal void on both T1- and T2-weighted MRI (Fig. 2). MRI was superior to CT in demonstrating the vertebral body bone marrow involvement (Fig. 2, bottom right). The effect of radiotherapy on the involved bone marrow was also better evaluated with MRI than with CT. The tumor borders and the surrounding soft tissue edema were clearly demonstrated on MRI. This was important for the evaluation of the tumor clinically because on palpation, the tumor was larger than the mass measured on CT and MRI. This was due to the edema that was not evident on CT examination.

Irradiation was chosen as a treatment option after the second operation because the patient was an adolescent. Although adequate radiation doses to control recurrent osteoblastoma have not been determined, it was assured that 5000 cGy would be a satisfactory dose. Although

the size of the tumor did not change radiologically, clinical symptoms responded promptly to radiation. After a silent period of 2 years, recurrence of symptoms forced us to choose chemotherapy as a treatment modality. After the first course of chemotherapy, pain was relieved and shrinkage of the lesion was observed. After six courses of therapy, the patient's clinical situation was perfect, although only partial response in the tumor size was observed. The patient has not received treatment for 18 months, and there has been no tumor regrowth or clinical symptoms.

Surgical excision remains the treatment of choice for primary or recurrent osteoblastoma. However, complete removal of the tumor may be technically difficult when it involves the vertebral column; such cases have been treated by curettage followed by radiation therapy [23]. There are few data about the role of chemotherapy. A short-term response to doxorubicin has been reported [24]. A long-term response to methotrexate, doxorubicin, and cisplatin has also been reported previously [21]. In selected patients with recurrent tumor, radiotherapy and chemotherapy might be useful as an additional treatment modality after incomplete excision of tumors. Also, radiotherapy and chemotherapy might be used in place of surgery for unresectable tumors and might render bulky, aggressive lesions more resectable.

REFERENCES

1. Dahlin DC (ed): "Bone Tumors: General Aspects and Data on 6,221 Cases." Charles C. Thomas, Springfield: 1978.
2. McLeod RA, Dahlin DC, Beabout JW: The spectrum of osteoblastoma. Am J Roentgenol 126:321–335, 1976.
3. Syklawer R, Osborn RE, Kerber W, Glass R: Magnetic resonance imaging of vertebral osteoblastoma: A report of two cases. Surg Neurol 34:421–426, 1990.
4. Azouz EM, Kozlowski K, Marton D, Sprague P, Zerhouni A, Asselah F: Osteoid osteoma of the spine in children. Pediatr Radiol 16:25–31, 1986.
5. Roessner A, Metze K, Heymer B: Aggressive osteoblastoma. Pathol Res Pract 179:433–436, 1985.
6. Jackson RP: Recurrent osteoblastoma: A review. Clin Orthop 131:229–232, 1978.
7. Kenan S, Floman Y, Robin GC, Laufer A: Aggressive osteoblastoma: A case report and review of the literature. Clin Orthop 195:294–298, 1985.
8. Mitchell ML, Ackerman LV: Metastatic and pseudomalignant osteoblastoma: A report of two unusual cases. Skel Radiol 15:213–218, 1986.
9. Merryweather R, Middlemiss JH, Sanerkin NG: Malignant transformation of osteoblastoma. J Bone Joint Surg [B] 62:381–384, 1980.
10. Pettine KA, Klassen RA: Osteoid-osteoma and osteoblastoma of the spine. J Bone Joint Surg [A] 68:354–361, 1986.
11. Amacher AL, Eltomey A: Spinal osteoblastoma in children and adolescents. Child Nerv Syst 1:29–32, 1985.
12. Azouz EM, Kozlowski K, Marton D: Osteoid osteoma and osteoblastoma of the spine in children: Report of 22 cases with brief literature review. Pediatr Radiol 16:25–31, 1986.
13. Myles ST, Mac Rae ME: Benign osteoblastoma of the spine in childhood. J Neurosurg 68:884–888, 1988.
14. Huvos AB (ed): "Bone Tumors: Diagnosis, Treatment and Prognosis." Philadelphia: WB Saunders, 1991.
15. Bertoni FD, Unni KK, Lucas DR: Osteoblastoma with a cartilaginous matrix: An unusual morphological presentation in 18 cases. Am J Surg Pathol 17:69–74, 1993.
16. Mirra JM, Kendick RA, Kendick RE: Pseudomalignant osteoblastoma versus arrested osteosarcoma. A case report. Cancer 37:2005–2006, 1976.
17. Schajowicz F, Lemos C: Osteoid osteoma and osteoblastoma. Closely related entities of osteoblastic derivation. Acta Orthop Scand 41:272–273, 1970.
18. Dorfman HD: Malignant transformation of benign bone lesions. Seventh National Cancer Conference Proceedings. Philadelphia: JB Lippincott, 1973.
19. Lucas DR, Unni KK, McLeod RA, O'connor MI, Sim FM: Osteoblastoma: Clinicopathologic study of 306 cases. Hum Pathol 25:117–134, 1994.
20. Kroon HM, Schurmans JS: Osteoblastoma: Clinical and radiologic findings in 98 new cases. Radiology 175:783–790, 1990.
21. Camitta B, Wells R, Segura A, Unni KK, Murray K, Dunn D: Osteoblastoma response to chemotherapy. Cancer 68:999–1003, 1991.
22. Nemoto O, Moser RP, Van Dam BE, Aoki J, Gilkey FW: Osteoblastoma of the spine. A review of 75 cases. Spine 15:1272–1280, 1990.
23. Shikata J, Yamamuro T, Hiokazu I, Kotoura Y: Benign osteoblastoma of the cervical vertebra. Surg Neurol 27:381–385, 1987.
24. Dorfman HD, Rosenthal DI, Mankin HJ, Fossburg MJ, Schiller AL: Case records of the Massachusetts General Hospital: Case 40-1980. N Engl J Med 303:866–873, 1980.